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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,071	02/14/2005	Isa Gokce	P69705US0	1733

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EXAMINER	
MONDESI, ROBERT B	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/501,071	GOKCE ET AL.	
	Examiner	Art Unit	
	Robert B. Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *14-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to restriction requirement

Applicants' election with traverse of Invention of Group I, **Claims 1-13** in amendment, filed July 3, 2006 is acknowledged. The traversal is on the ground(s) that **claim 1** is drawn to a fusion polypeptide having a ToAIII domain as the only functional domain and the cited reference (WO 01/21817) does not provide the suggestion for a skilled artisan to use the TolAIII domain as fusion partner for improvement of recombinant protein production. This is not found persuasive because the scope of **claim 1** includes the recited fragments of a fusion protein comprising the TolAIII domain and WO 01/21817 discloses fragments of TolAIII. Furthermore the claims are not drawn to a method of using the product but rather are to drawn to the actual product and therefore the indented use of the product is not the determining factor with regards to prior art considerations. In other words the prior art structure is capable of performing the intended use, then it meets the claim. Wan et al., 1998 disclose a fusion protein comprising the TolAIII domain and further comprising an N-terminal signal sequence wherein the said fusion polypeptide has been optimized for expression in a host cell (page 16, column 2, paragraph 2, lines 22).

Therefore the requirement is still deemed proper and is made FINAL. **Claims 1-36** are pending in this application. **Claims 14-36** are withdrawn from further consideration because these Claims are drawn to non-elected inventions (Note to applicants, after further consideration the examiner has determined that **claim 14** is

drawn to a DNA molecule and belongs in Group II). **Claims 1-13** are currently under examination.

Priority

The current application filed on February 14, 2005 a 371 of PCT/GB03/00078 filed January 10, 2003 claims priority to a foreign application, UNITED KINGDOM 0200689.8 January 10, 2002. A certified copy of foreign document UNITED KINGDOM 0200689.8 has been provided.

Preliminary Amendment

The preliminary amendment filed July 9, 2004 has been entered.

Drawings

Drawings filed July 9, 2004 have been accepted.

Information Disclosure Statement

The IDS filed October 14, 2004 has been received and is signed and considered, a copy of the PTO 1449 is attached to the following document.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to functional homologue/derivatives/fragment of TolAIII. The claims do not require that the polypeptide possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to a genus of polypeptides that is defined by an unclear functional relationship to TolAIII. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a partial structure in the form of a recitation a relationship to the domain of a peptide designated as TolAIII. The specification does not identify any particular portion of the structure that must be characteristics of the claimed genus are not described. The only adequately described species is TolAIII and no active variants are disclosed. Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the a14 that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed." (See page 1117.) The specification does not it clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116), As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers* v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF' s were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only TolAIII, but not the full breadth of the claim meets the written description provision of 35 U. S.C. 112, first paragraph. Applicant is reminded that *Vas-cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision.

Furthermore as amended **claim 1** contains new matter. Applicants' have amended **claim 1** to include the phrase " a basic structure in sequence, an N-terminus"

however there is no discussion of a N-terminus that has a basic structure in sequence, as in for example containing lysine or histidine, in specification of the present application.

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In **claim 1**, the phrase "a basic structure, in sequence, an N-terminus" fails to make sense. It appears that the applicants are insinuating that there is particular order to the hybrid structure of the claimed fusion protein wherein there is an N-terminus, the TolAIII domain, followed by a C-terminus non-TolA protein (see page 3, paragraph 5, lines 1-5 of the specification of the instant application); however as stated it is not clear if it is meant that the actual sequence present on the N-terminus region of the fusion protein is "basic in structure" as in being composed from basic amino acids such as : Arginine, Lysine or Histindine. Applicants need to amend the claim and clarify the mentioned ambiguity in order to overcome the rejection.

In **claims 1 and 13** applicants have used the terms TolAIII and BCL-XL to define particular amino acid sequences; however the said terms are laboratory designations and are not sufficient to describe specific amino acid sequence. Applicants need to use a sequence identifier, as in a SEQ ID NO:, in order to define the mentioned ammo acid sequences.

In **claims 1 and 10**, applicants have used the term "optionally", it is not clear as to whether the limitations following the said term are encompassed by the intended

breadth of the claims. **Claims 2-13** are dependent claims that do not remedy the deficiencies of the independent claim that they are dependent therefrom.

In **claims 1, 4-5, 11 and 13** needs to be spelled out in the first instance of use.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, **claim 10** recites the broad recitation one or more, and the claim also recites "preferably n=6" in line 3 and "preferably 2", line 4 which are the narrower statement of the range/limitation.

Regarding **claim 12**, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

In **claim 11**, the applicants have stated that the TolAIII domain consists of amino acid residues 329-421 of SEQ ID NO: 13; however SEQ ID NO: 13 consists of only 93 residues.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-13 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The polypeptide as claimed, has an amino acid sequence duplicative of that of the of a fusion polypeptide comprising the ToAIII domain or the cellular precursor thereof and possesses the biological and functional properties of the naturally occurring fusion polypeptide comprising the ToAIII and therefore does not constitute patentable subject matter absent recitation of "isolated and purified" in the preamble.

See *American Wood v. Fiber Disintegrating Co.*, 90 U. S. 566 (1974); *American Fruit Growers v. Brogdex Co.*, 283 U. S. 1 (1931); *Funk Brothers Seed Co. v. Kalo Inoculant*, 33 U. S. 127 (1948); and *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Claims 1-13 as written, do not sufficiently distinguish over host cells that exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, he naturally occurring products are considered nonstatutory subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U. S.

566 (1974); *American Fruit Growers v. Brogdex Co.*, 283 U. S. 1 (1931); *Funk Brothers Seed Co. v. Kalo Inoculant*, 33 U. S. 127 (1948); and *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or purified". See MPEP 2105.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 01/21817 (cited in the IDS filed July 9, 2004).

WO 01/21817 discloses a fusion polypeptide, wherein the said fusion polypeptide comprises a TolAIII domain attached to a non-TolA protein partner (page 7, lines 26-29 through page 8, lines 1-5).

Thus WO 01/21817 teaches all the elements of **claims 1 and 11-12** and these claims are anticipated under 35 USC 102(b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/21817 (cited in the IDS filed July 9, 2004) in view of Wan et al., 1998 (cited in the IDS filed July 9, 2004).

WO 01/21817 discloses a fusion polypeptide as mentioned above.

WO 01/21817 does not teach that the fusion polypeptide comprises an N-terminal signal sequence or that the said fusion polypeptide has been optimized for expression in a host cell.

Wan et al. disclose a fusion protein comprising the TolAIII domain and further comprising an N-terminal signal sequence wherein the said fusion polypeptide has been optimized for expression in a host cell (page 16, column 2, paragraph 2, lines 22).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to fuse an N-terminal signal sequence to a fusion polypeptide comprising the TolAIII domain for the advantages of the secretion of the expressed

recombinant product as taught by WO 01/21817 and Wan et al., see Wan et al. at page 20, column 1, paragraph 2 lines 1-14.

Claims 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/21817 (cited in the IDS filed July 9, 2004) in view of Mai et al., US Patent No. 5,087,564.

WO 01/21817 discloses a fusion polypeptide as mentioned above.

WO 01/21817 does not teach that the mentioned fusion polypeptide comprises a linker between the TolAIII domain and the non TolAIII domain wherein the linker comprises at least one cleavage site for an endopeptidase.

Mai et al. teach of linkers used in fusion polypeptides comprising at least one cleavage site for an endopeptidase (column 8, lines 12-25).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to place linkers comprising enopeptidase cleavage sites inside a fusion protein advantages of site specific release of desired peptide., as taught by WO 01/21817 and Mai et al., see Mai et al., at column 6, lines 60-64.

Claims 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/21817 (cited in the IDS filed July 9, 2004) in view of Derouiche et al., 1997 (cited in the IDS filed July 9, 2004).

WO 01/21817 discloses a fusion polypeptide as mentioned above.

WO 01/21817 does not teach that the mentioned fusion polypeptide further comprises an N-terminal poly His tag.

Derouiche et al. disclose a fusion polypeptide comprising a TolAIII domain further comprising an N-terminal poly His tag (page 3187, column 1, paragraph 4, lines 5-7).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to fuse an N-terminal poly His tag to a fusion polypeptide comprising the TolAIII domain for the advantages of the ease of purification, as taught by WO 01/21817 and Derouiche et al., see Derouiche et al., at page 3190, column 1, paragraph 4, lines 1-6.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/21817 (cited in the IDS filed July 9, 2004) in view of Mark et al. US Patent Publication No. 2002/0137049.

WO 01/21817 discloses a fusion polypeptide as mentioned above.

WO 01/21817 does not teach that the mentioned fusion polypeptide comprises BCL-XL.

Mark et al., disclose a fusion protein that comprises BCL-XL (page 4, paragraph 0063, lines 1-19).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to fuse a BCL-XL domain to a fusion polypeptide comprising the TolAIII domain for the advantages of the ability to modulate neural cell processes, as taught by WO 01/21817 and Mark et al., see Mark et al., at page 1, paragraph 005, lines 1-6.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B. Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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